Hypertension and obstructive sleep apnoea

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Abstract:
Obstructive Sleep Apnoea (OSA) is the main variable risk element of hypertension and patients of hypertensive having Obstructive Sleep Apnoea have high risk for CVD (cardiovascular disease). It has been revealed by significant number of researches that hypertension and obstructive sleep apnoea have synergistic effects on the system of cardiovascular and thus it is relevant and important clinically to enhance the knowledge of interaction of pathophysiology between hypertension and obstructive sleep apnoea. In the current study, after brief review of the pathophysiological effects and characteristics of obstructive sleep apnoea, the focus will be on the understanding of obstructive sleep apnoea connected hypertension, the important ways for treating obstructive sleep apnoea and treatment effects of obstructive sleep apnoea on managing hypertension. We are of the view that the current study will bring light for the upcoming researches that explore effective therapeutic planning for the improvement of management of hypertension and obstructive sleep apnoea.

Keywords: Hypertension, obstructive, sleep apnoea

INTRODUCTION
It is well settled that the second common reason for elevating blood pressure is the obstructive sleep apnoea. Furthermore, the patients of hypertensive with obstructive sleep apnoea have high risk of growing resistant hypertension and experience the changes of cardiovascular and comparison of the events with hypertensive patients without obstructive sleep apnoea. Most importantly, it has been found that ~ 50% patients of obstructive sleep apnoea suffering from hypertension and ~30% patients of hypertension have obstructive sleep apnoea. Therefore, it imperative to diagnose, identify and treat obstructive sleep apnoea for the effective improved control of hypertension and to decrease the prevalence and incidence of cardiovascular diseases related to hypertension. In the recent era, the studies based on population have shown that hypertension and obstructive sleep apnoea are placing health and economic burdens on patients individually and society. Moreover, because of huge clinical and experimental researches, the evidence is accumulating relating to the synergistic effects which hypertension and obstructive sleep apnoea exercise on the system of cardiovascular. Thus, we are of the view that in order to manage and understand the diseases efficiently and effectively, it is clinically significant to examine the interactions of pathophysiology between hypertension and obstructive sleep apnoea.

In the current review, the following aspects are focused; obstructive sleep apnoea characteristics, obstructive sleep apnoea’s general effects of pathophysiology on the system of cardiovascular and elaborate the main mechanism with which obstructive sleep apnoea is adding to the pathogenesis of arterial hypertension and other groups of hypertensions connected with obstructive sleep apnoea. Lastly, potential approaches have been presented to manage obstructive sleep apnoea and its improvement effect in the reduction of the Blood Pressure.

DEFINITION, DIAGNOSIS AND RISK FACTORS OF OSA
Obstructive sleep apnoea is occurring night-time sleep and its diagnose need polysomnography to measure main elements like chest and abdomen respiratory movement, arterial oxygen saturation, quantified air flow and electroencephalogram; subsequently all these indexes are used for determining the index of apnoe-hypopnoea. In short, the index of apnoe-hypopnoea is the all incidence of apnoea (total airflow obstruction for >10s) and hypopnoea (decrease of respiratory airflow to 450% along with decrease of 43% of arterial oxygen saturation for >10s) per hour of sleep; the classification of OSA patients in the categories of 5-15 mild, 15-30 moderate and severe (430). Besides the index of apnoe-hypopnoea, obstructive sleep apnoea typical clinical symptoms such as frequently awake during sleep, sleepiness during daytime and fatigue, nocturia, snoring, impaired memory and decreased concentration are the significant signs for diagnose clinically. Recently, several studies have found numerous sensitive predictors which are beneficial in pointing out the increased-risk population. For instance, patients having abnormal anatomy of upper airway (like collapse of pharyngeal because of macroglossia and adeno tonsillar hypertrophy or...
displacement of tongue and narrowing of pharynx because of retrognathia), that non-obese people and Asian are predisposed to, can grow obstructive sleep apnoea. Studies of epidemiology have revealed that men are inclined to obstructive sleep apnoea, and chances of growing obstructive sleep apnoea steadily rise with age and weight gain. Hereditary elements have also part in the development of obstructive sleep apnoea, as it stated by Buxbaum et al. Lastly, alcohol abuse, smoking, nasal congestion and hormone depletion in postmenopausal because of allergic rhinitis are too regarded as risk elements for obstructive sleep apnoea, obstructive sleep apnoea. The prevention of obstructive sleep apnoea growth is difficult due to the increased prevalence of obstructive sleep apnoea in the people. Therefore, considering the common risk elements and obstructive sleep apnoea normal clinical manifestations (Figure 1) are significant for timely pointing out the unidentified obstructive sleep apnoea population and appropriate use of polysomnography is beneficial for diagnosing precisely and assessment of the obstructive sleep apnoea severity.

PATHOPHYSIOLOGICAL EFFECTS OF OSA ON THE CARDIOVASCULAR SYSTEM

By way of different mechanisms, the pathophysiological effects are conferred by obstructive sleep apnoea on the cardiovascular system (Figure No.2). Additionally, deprivation of sleep and numerous arousals because of periodic asphyxia are causing sympathetic nerve activation and adding to hypertension and tachycardia. With the passage of time, these changes of hemodynamic are finally resulting in heart failure and left ventricular hypertrophy. Secondly, it is found that hypoxemia is promoting systemic inflammation, oxidative stress and endothelial dysfunction, which is collectively adding to the growth of atherosclerotic cardiovascular diseases. Thirdly, negative intra-thoracic stress is produced for counteracting with the narrowing pharynx and it also enhances the mechanical pressure on the atra and ventricles. The remodeling of cardiac (which includes left atrial enlargement and left ventricle hypertrophy) occurs and the changes of maladaptive can show finally as an obvious cardiovascular disease like atrial fibrillation and diastolic heart failure. Lastly, cardiovascular disorder connected with obstructive sleep apnoea is also contributed by pathophysiological effects such as incessant activation of the renin-angiotensin-aldosterone axis and impaired baroreflex sensitivity. Collectively, the notion has strong support by the gathered clinical data that in pathogenesis of cardiovascular disease the obstructive sleep apnoea has main role; it is important clinically to have effective control of obstructive sleep apnoea in order to lessen the adverse effects of obstructive sleep apnoea communicate on the system of cardiovascular.

PATHOPHYSIOLOGICAL MECHANISMS OF OSA HYPERTENSION

The obstructive sleep apnoea relation with hypertension has been thoroughly examined and there is strong evidence to point out that there is exist dose-effect relation between the elevation degree of BP and severity of obstructive sleep apnoea. The pathophysiological mechanism is multifactorial with which obstructive sleep apnoea is contributing to the elevation of BP. One the one side, obstructive sleep apnoea induced hypoxemia results in oxidative stress and systemic inflammation, which ended in high endothelin-1 production and reduced nitric oxide generation in endothelial cell, BP elevation and enhanced arterial peripheral resistance. On the other, frequent arousals, periodic hypoxemia and deprivation of sleep causing the activation of sympathetic nerve which is leading to the peripheral vessel constriction and enhanced cardiac output, thus is promoting the elevation of BP. The obstructive sleep apnoea patients are reported to have increased incidence of isolated diastolic hypertension and the basic mechanism may be because of cardiac diastole shortening and tachycardia. Thirdly it is stated that patients with obstructive sleep apnoea have considerably higher renin production caused by efferent renal sympathetic nerve activation and this effect is leading towards the increase in aldosterone and plasma angiotensin-II. Collectively, the effects are causing the elevation of BP by means retention of sodium-water and vasoconstriction. It is further reported that there is increased prevalence of primary hyperaldosteronism in the obstructive sleep apnoea patients; thus, it is imperative to have screening for primary hyperaldosteronism. The study has also reported that there is more likelihood of development of drug-resistant hypertension among the obstructive sleep apnoea and primary hyperaldosteronism patients. It is further reported that the deprivation of sleep from obstructive sleep apnoeas connected with arterial stiffness and endothelial dysfunction, both are causing the acceleration and initiation of the hypertension development. The proposed mechanisms are mentioned in Figure 3 with which obstructive sleep apnoea is causing hypertension. The obstructive sleep apnoea’s pathophysiological effect on the hypertension are of multi factor and it is because of the obstructive sleep apnoea’s increased prevalence..
in the patients of hypertension. We are of the opinion that obstructive sleep apnoea improvement must have an outcome with great benefits in the management of hypertension.

**DIFFERENT CATEGORIES OF HYPERTENSION RELATED TO OSA**

A considerable amount of epidemiological researches have shown that there are special classes of OSA related hypertension; the most common and relevant clinically classes are nocturnal hypertension, resistant hypertension and masked hypertension.

**OSA and resistant hypertension**

Resistant hypertension is defined as Blood Pressure which stays more than 140/90mm Hg in spite of the treatment with 3 different categories of medicine anti-hypertension (inclusive of diuretics) at its best dose, is a obstructive sleep apnoea’s common secondary effect. For instance, it has been observed by Calhoun et al. that resistant hypertension patients (male 90% and female 77%) have obstructive sleep apnoea. According to study carried out by Ruttenaumppawan et al., it has been reported that obstructive sleep apnoeas connected with the high risk of resistant hypertension, with an adjusted 1.025 odds ratio (95% confidence interval of 1.002-1.049). Further, 2 cross-sectional researches have shown that there exists relationship of dose-effect between the BP rise magnitude and severity of obstructive sleep apnoea, and also the quantity of medicine anti-hypertensive for managing the hypertension. Recently, a clinically research has shown that obstructive sleep apnoea clinically significant is independently connected with concentric hypertrophy Figure 1. Algorithm diagnostic and screening for obstructive sleep apnoea in resistant hypertension patients suggests that obstructive sleep apnoea may quicken the adverse remodelling of cardiovascular in the resistant hypertension patients.

A good amount of mechanisms added to the resistant hypertension related to obstructive sleep apnoea. Further, besides the above-mentioned obstructive sleep apnoea’s pathophysiological effects which can result in elevation of BP, primary hyperaldosteronism is also considered one of the reasons for the phenomena. Primary hyperaldosteronism is reported to have high prevalence among the patients of resistant hypertension and associated obstructive sleep apnoea; findings reveal that patients with these have urine and plasma level of aldosterone considerably high. Retention of water and sodium by hyperaldosteronism can result in elevation of BP and overload volume whereas para pharyngeal oedema caused by retention of fluid can worsen obstructive sleep apnoea and promote the elevation of BP. It has been suggested by the earlier studies that vicious cycle can be interfered by treating with aldosterone antagonists and Continuous Positive Airway Pressure (CPAP) therapy. Although, randomly controlling of clinical trials are still required to give proper evidence that therapeutic modalities can support to have better control of BO in the resistant hypertension patients. Moreover, it is also imperative to investigate the benefits of cardiovascular of these therapies.

**OSA and nocturnal hypertension**

As per the BP patterns of circadian, high blood pressure can be categorised in types: non-dipping and dipping. Succinctly, pattern of dipping is over 10% reduction in night-time blood pressure than the day-time. On the contrary, the presence of nocturnal hypertension is where below 10% decrease (non-dipping) in blood pressure at night or when the night-time blood pressure is more than the day-time. It has been found by several earlier studies that there is great adverse effect of nocturnal hypertension on the system of cardiovascular as compared to day-time hypertension. It has also been found that there is high prevalence of nocturnal hypertension in obstructive sleep apnoea patients. For instance, it has been reported by Loredo et al. that in the study ~ 84% obstructive sleep apnoea patients experienced nocturnal hypertension. It has been pointed out from the data of Wisconsin Sleep Cohort that there is relationship of dose-effect between the elevation risk of night-time blood pressure and the obstructive sleep apnoea severity. The key mechanism adding to the elevation of night-time blood pressure is the frequent arousals, sympathetic overactivation caused by hypoxemia and sleep deprivation. Elevation of night-time blood pressure can be reversed with Obstructive sleep apnoea treatment with CPAP therapy. It is clinically significant to screen obstructive sleep apnoea in the patients non-dipping or hypertension not easy to treat.

**OSA and masked hypertension**

The term masked hypertension is used to explain the condition when blood pressure assessed in office falls with range, but blood pressure measured at home or by 24 hours ambulatory it is more than the normal range. According to Baguet et al. in his epidemiological research showed that there is 30% prevalence of masked hypertension in the patients who are newly diagnosed obstructive sleep apnoea. Other study has shown that in the
group of 61 male patients identified as normotensive by clinical assessment of blood pressure, out of them 1/3rd were with masked hypertension and obstructive sleep apnoea patients had high prevalence of masked hypertension as compared to patient without obstructive sleep apnoea. This shows the existence of special connection between masked hypertension and obstructive sleep apnoea; however, several prospective researches are required to corroborate these results and to assist the physician in identifying the patients with high risk of masked hypertension.

**APPROACHES FOR MANAGING OSA-ASSOCIATED HYPERTENSION**

Besides the drugs of anti-hypertension, there is some other more effective non-pharmacologic ways to treat hypertension connected with obstructive sleep apnoea. For instance, better control of co-morbidities which add to obstructive sleep apnoea and hypertension like smoking, obesity and alcohol abuse, are regarded as the best cost-effective strategy.

Blood pressure in hypertensive patient with obstructive sleep apnoea can be reduce by the CPAP therapy and oral appliances. Clinical researches have shown that the benefits of oral appliance therapy is not limited to improvement of obstructive sleep apnoea but also for decreasing the blood pressure. Recently, Andrén et al. in random trial assessed 72 patients with hypertension and obstructive sleep apnoea, they randomly receive either control treatment or wearing appliance for three months with mandibular advancement. It has been shown by Drager et al. that in hypertensive or prehypertensive patients with obstructive sleep apnoea, treatment of CPAP significantly decreases the day-time systolic BP and night-time systolic blood pressure and diastolic blood pressure while comparing with the control group. CPAP therapy, in recent published meta-analysis, was considerable connected with 24 hours ambulatory systolic blood pressure and diastolic blood pressure decrease. Furthermore, CPAP appears to be more benefiting for the reduction of night-time systolic blood pressure as compared to diurnal systolic blood pressure, and resistant hypertension patients appears to get more advantage from CPAP therapy.

Succinctly, the deriving of benefits from the treatment of CPAP may be connected with the amelioration of hypoxemia and reduced nocturnal sympathetic nervous activation, and consequential betterments in the arterial oxygen saturation can make less severe the systemic inflammation and oxidative stress. Furthermore, decreased negative intra-thoracic pressure due to the positive ventilation pressure can also end in the advantageous hemodynamic alterations. All beneficial effect of the treatment of CPAP concurrently improve the control of hypertension.

It has been shown in the recent clinical research that a single pre-CPAP treatment bunch of 3 plasma micro RNAs forecated the blood pressure response to the treatment of CPAP in resistant hypertension and obstructive sleep apnoea patients; in future, CPAP therapy in hypertensive and obstructive sleep apnoea patients can be assisted in targeting by the precision medicine using microRNA measurement. There is no solid proof of apnoea-hypopnea index betterment with anti-hypertensive medicine such as angiotensin receptor blocker or angiotensin-converting enzyme inhibitor, diuretic, calcium channel blocker, β-blocker and α-receptor antagonist. Furthermore, diuretic may enjoy the important role in controlling the blood pressure by improving the para pharyngeal oedema. Generally, the patients with hypertension connected with obstructive sleep apnoea are recommended to treat with a combination of different therapeutic modalities.

**CONCLUSION**

Screening for obstructive sleep apnoea in the patients of hypertension is clinically significant especially patients showing predominant elevation of diastolic blood pressure, difficult in controlling blood pressure and elevation of nocturnal blood pressure. Enhancement of understanding and knowledge with regard to interplay of the mechanism of hypertension and obstructive sleep apnoeas critical for having efficient control of hypertension connected with obstructive sleep apnoea. More research is required specially in precision medicine to examine the effective therapeutic planning for the improvement of management of hypertension and obstructive sleep apnoea.

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